

Applicant : Masayuki iya et al.  
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REMARKS

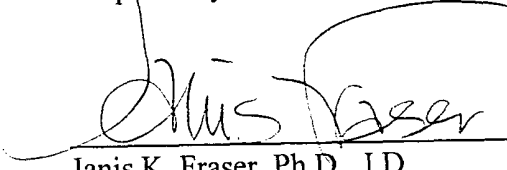
Claims 1-40 are pending, claims 3-9, 14, 16, 17, 24, 25, 27, 28, and 36-40 having been amended to delete multiple dependency. No new matter has been added.

Attached is a marked-up version of the changes being made by the current amendment. Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date:

April 20, 2001

  
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**Version with markings to show changes made**

**In the specification:**

Paragraph beginning at page 11, line 27 has been amended as follows:

An *E. coli* strain containing plasmid TABI-f-4, which comprises a DNA encoding a human TAB1 peptide having the amino acid sequence from Met at amino acid 1 to Pro at amino acid 504 in the TAB1 amino acid sequence shown in SEQ ID NO: 4, was named *Escherichia coli* DH5[a]α (TABI-f-4) and has been deposited internationally under the Budapest Treaty as an accession No. FERM BP-5599 in The National Institute of Bioscience and Human-Technology, The Agency of Industrial Science and Technology (1-1-3 Higashi, Tsukuba, Ibaraki, Japan) on July 19th, 1996.

**In the claims:**

Claims 3-9, 14, 16, 17, 24, 25, 27, 28, and 36-40 have been amended as follows:

3. (Amended) The method of claim 1[ or 2], wherein the TAK1 or the TAB1 is linked to a support.

4. (Amended) The method of [any one of claims 1 to 3] claim 1, wherein a label is attached to the TAK1 or the TAB1 and wherein the binding is detected by detecting or measuring the label.

5. (Amended) The method of [any one of claims 1 to 3] claim 1, wherein the binding is detected by detecting or measuring the TAB1 bound to the TAK1 with a primary antibody against TAB1 or a primary antibody against the peptide fused with the TAB1.

6. (Amended) The method of [any one of claims 1 to 3] claim 1, wherein the binding is detected by detecting or measuring the TAK1 bound to the TAB1 with a primary antibody against TAK1 or a primary antibody against the peptide fused with the TAK1.

7. (Amended) The method of [any one of claims 1 to 3] claim 1, wherein the binding is detected by detecting or measuring the TAB1 bound to the TAK1 with a primary antibody against the TAB1 or a primary antibody against the peptide fused with TAB1, and a secondary antibody against the primary antibody.

8. (Amended) The method of [any one of claims 1 to 3] claim 1, wherein the binding is detected by detecting or measuring the TAK1 bound to the TAB1 with a primary antibody against TAK1 or a primary antibody against the peptide fused with the TAK1, and a secondary antibody against the primary antibody.

9. (Amended) The method of [any one of claims 5 to 8] claim 5, wherein the primary antibody or the secondary antibody is labeled with radioisotope, enzyme, or fluorescent substance.

14. (Amended) The method of claim 12[ or 13], wherein a substrate for the TAK1 is added and wherein the phosphorylation of the substrate by the TAK1 is detected.

16. (Amended) The method of [any one of claims 12 to 15] claim 12, wherein the TAK1 is fused with a peptide.

17. (Amended) The method of [any one of claims 12 to 16] claim 12, wherein the TAK1 is linked to a support.

24. (Amended) The method of claim 20[ or 23], wherein the reporter gene is luciferase, chloramphenicol acetyltransferase, green fluorescent protein, or  $\beta$ -galactosidase.

25. (Amended) The method of [any one of claims 18 to 24] claim 18, wherein an inflammatory stimulus is given to cells and wherein the biological activity transduced through TAK1 or through TAK1 and TAB1 is detected and/or measured.

27. (Amended) The method of [any one of claims 1 to 26] claim 1, wherein the inflammatory cytokine is IL-1, TNF, IL-10, or IL-6.

28. (Amended) A compound for inhibiting signal transduction through inflammatory cytokines, the compound that can be isolated by the method of [any one of claims 1 to 27] claim 1.

36. (Amended) The pharmaceutical composition of [any one of claims 33 to 35] claim 33, wherein the pharmaceutical composition is an anti-inflammatory agent.

37. (Amended) The pharmaceutical composition of [any one of claims 33 to 36] claim 33, wherein the compound is a compound inhibiting binding between TAK1 and TAB1.

38. (Amended) The pharmaceutical composition of [any one of claims 33 to 36] claim 33, wherein the compound is a compound inhibiting phosphorylation by TAK1.

39. (Amended) The pharmaceutical composition of [any one of claims 33 to 38] claim 33, wherein the compound is a compound that can be isolated by the [method of any one of claims 1 to 27] steps of:

(a) contacting a test sample with TAK1 and TAB1:

(b) detecting binding between the TAK1 and the TAB1; and

(c) selecting a compound inhibiting the binding.

40. (Amended) The pharmaceutical composition of [any one of claims 33 to 39] claim 33, wherein the inflammatory cytokine is IL-1, TNF, IL-10, or IL-6.